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COGNITIVE PROFILE IN HEART FAILURE AND HYPERTENSION

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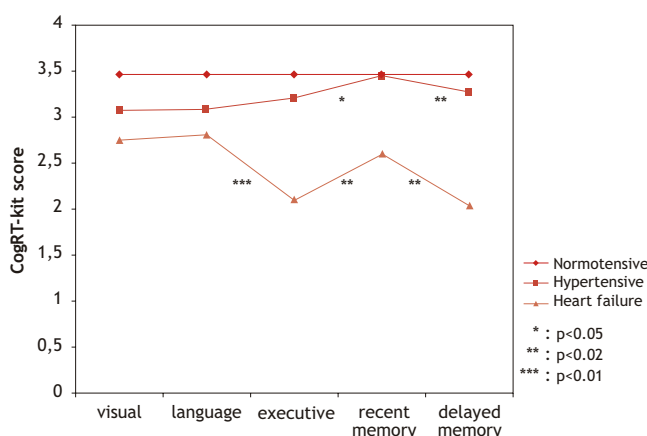
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Objective — To assess and compare cognitive levels and profiles of five cognitive functions according to hypertensive and heart failure status.

Methods — 111 hypertensive patients (24h-Ambulatory Blood Pressure Monitoring: day-systolic BP >135 mmHg, day-diastolic BP >85 mmHg, night-systolic BP > 120 mmHg or night-diastolic BP > 70 mmHg), 56 normotensive patients and 51 stable heart failure patients (Left Ventricular Ejection Fraction <45%) all French speaking and without previously known dementia, depression (Beck Depression Inventory >21) or recent stroke, underwent a computerized cognitive test: the CogRT-Kit. This new neuropsychological test evaluates globally and specifically 5 cognitive functions (visuospatial abilities, language, executive functions, recent and delayed memory) with the same paradigm. Therefore this test enhances comparison between functions to determine a cognitive profile. Comparison between function in profile used the Student t-test.

Results — Heart failure was significantly associated with global cognition ($\beta=-0.65$, $p=0.04$, $R^2=0.27$), language, ($\beta=-0.56$, $p=0.002$, $R^2=0.26$) executive functions ($\beta=-0.96$, $p=0.007$, $R^2=0.34$) recent ($\beta=-0.75$, $p<0.001$, $R^2=0.33$) and delayed memory ($\beta=-0.95$, $p=0.001$, $R^2=0.22$) in multivariate analysis after adjustment on age, gender, years of education and hypertension.

A subgroup analysis on 60-75 years old patients, 41 hypertensive, 19 heart failure and 33 normotensive patients matched on age, years of education and gender, was performed. No significant difference on depression index, exposure to anxiolytics/hypnotics, sleep-apnea syndrome and other cardiovascular risk factors was observed. The cognitive profile (Fig 1) shows significant level differences between functions in heart failure compared to normotensive (normalized) with significant deficits in executive functions ($p<0.01$) and delayed memory ($p<0.02$), while cognitive functions are affected with the same level in hypertension except for recent memory.



Conclusion — We confirm that heart failure is an independent predictor of cognitive impairment, and affects more specifically language, executive functions, recent and delayed memory. Hypertension slightly impairs cognitive functions with the same level.

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INSIGHTS INTO THE GENETIC AND CELLULAR CONTROL OF PROXIMAL CORONARY ARTERY PATTERNING

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In humans, TBX1 is the major candidate gene for DiGeorge (del22q11.2) syndrome, which includes heart malformations such as tetralogy of Fallot and Persistent Truncus Arteriosus (PTA). In Tbx1 null embryos, Second Heart Field (SHF) cardiac progenitor cell numbers are decreased leading to a hypoplastic outflow tract and PTA. Recently, we have shown that the Tbx1 phenotype is associated with reduction of a specific progenitor cell population that normally contributes to myocardium at the base of the pulmonary trunk. The Tbx1 mutant ventricular outlet thus has a predominantly subaortic identity supported by the presence of a single outflow valve with three leaflets. In addition, we demonstrated that coronary artery patterning is abnormal in Tbx1-nulls. Proximal coronary arteries course abnormally across the ventral region of mutant hearts and left and right arteries branch to the right/ventral sinus of the common outlet.

Coronary artery patterning defects are observed at early developmental stages at the level of the coronary plexus suggesting that SHF derived cells influence the cellular and molecular events responsible for the distribution and branching of proximal coronary arteries. We have identified Semaphorin3c as a Tbx1-dependent gene expressed in subpulmonary myocardium. However, Sema3c-null embryos do not show major coronary artery defects suggesting that Sema3c function overlaps with that of other genes affected in Tbx1 mutant embryos. We are now investigating the distribution and patterning of additional vascular guidance molecules as well as the distribution of neural crest cells and cardiac cushions which play critical roles in outflow tract development in wild type mice.

Our results provide new insights into the association between conotruncal defects and coronary artery anomalies and implicate SHF derived cells in coronary artery patterning. Ongoing research in collaboration with Necker Hospital (Paris) aims to investigate whether specific coronary artery anomalies are associated with PTA in DiGeorge syndrome.

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L'ALTÉRATION CONTRACTILE SOUS-ENDOCARDIQUE EST PRÉSENTE DANS UN MODÈLE CANIN DE DYSTROPHIE MUSCULAIRE DE DUCHENNE ET APPARAÎT COMME UN PHÉNOMÈNE CELLULAIRE INTRINSÈQUE

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